both challenges and opportunities for industry. The changes in the DSM-5 criteria may translate into changes for how we go about developing medical products to treat psychiatric disorders, including ADHD. There will need to be an investment in research and education, and sponsors must examine the possibility of developing new endpoints and outcome assessments for use in clinical trials.

PRM185
THE IMPACT OF DSM-5 ON THE DEVELOPMENT OF DRUGS TO TREAT MAJOR DEPRESSIVE DISORDER
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OBJECTIVES: In May 2013, the American Psychiatric Association released the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), a classification system for psychiatric conditions. DSM-5 brings significant changes to many diagnostic categories as compared to the previous edition. The objective of this review was to examine the changes in the Major Depressive Disorder (MDD) criteria and discuss the impact these changes may have for industry. **METHODS:** A line-by-line review of the DSM-5 and DSM-IV criteria for MDD was undertaken. Significant changes were highlighted and discussed from the point of view of sponsors of clinical trials for psychopharmacologic agents being developed to treat MDD. **RESULTS:** The primary symptom criterion for MDD remains unchanged, requiring five of nine symptoms, over a two-week period. The changes of note have to do with the differential diagnoses and specifiers. One change that received significant attention in the time leading up to the publication of DSM-5 was the elimination of the bereavement exclusion, which discounted bereavement after the loss a loved one within the first two months as part of the normal grief process. In terms of specifiers, a new addition in MDD is "with anxious distress," referring to episodes of depression characterized by at least two of five symptoms of anxiety. DSM-5 notes that this is associated with "greater likelihood of treatment nonresponse." Therefore, this is a factor sponsors may wish to consider in developing their trial inclusion/exclusion criteria. **CONCLUSIONS:** The significant changes in DSM-5 pose both challenges and opportunities for industry. The changes in the DSM-5 criteria translate into changes for how we go about developing medical products to treat psychiatric disorders, including MDD. There will need to be an investment in research and education, and sponsors must examine the possibility of developing new endpoints and outcome assessments for use in clinical trials.

PRM186
PATIENT NETWORKS AS A DATA SOURCE FOR PATIENT REPORTED OUTCOMES RESEARCH. CARENITY EXPERIENCE
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OBJECTIVES: To explore the potential of online patient networks (PN) as a viable source of PRO data for clinical research. Several PNs have emerged in the last few years in different European countries, and as a natural meeting point for chronic patients with an active engaged with their communities, they represent a promising source of patient reported data. In this original, the experience with the French PN "Carenity" is described. **METHODS:** Given the great heterogeneity of the users of "Carenity", and the fact that the test was computer-led by definition, a Computer Adaptive Test (CAT) was considered the best choice. The authors decided to use a culturally adapted version of CAT-Health system, which measures generic health-related quality of life (HRQoL). However, in absence of a calibration for the French population, a selection of the best items was used, using the Spanish calibration as a reference. All patients in the PN were invited to participate in the test. A score was estimated for the test using the Spanish parameters, as a rough approximation of the real score. Age, sex and the main pathology of the subjects were also collected. **RESULTS:** Preliminary results from the first week of data collection show 601 patients answered (Women: 404, Men: 140). The most frequent reported pathologies and their t-scores were multiple sclerosis (N:92,M:37.91,SD:5.85), fibromyalgia (N:81,M:36.65,SD:4.99), ankylosing spondylitis(N:60,M:37.74,SD:5.32) and both types of diabetes (I: N:53,M:50.38,SD:10.94, II: N:41,M:48.12,SD:10.04). Significant differences ($p<0.05$) were found in diabetes patients by sex, and between both types of diabetes and the other 3 most common pathologies. **CONCLUSIONS:** Carenity PN seems to be a fast way to obtain PRO scores directly from patients. Preliminary results show differences in the expected direction.

RESEARCH ON METHODS – Statistical Methods

PRM187
DEFINING THE PROPER METHODOLOGY TO USE IN A DATA-PEEK FOR POWER (DPP)
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OBJECTIVES: Late phase research is conducted outside the RCT setting where there is uncertainty as to how many subjects are needed to find differences between groups. Due to the lack of real-world information (non-RCT) in late phase designs, there are no tangible inputs for power calculations. This research defines a bias-free method to examine data while determining sample size. **METHODS:** As an example of the application of a DPP, a study examining the decrease of HGbA1c values in two different insulin delivery methods was examined in patients with several comorbid conditions. Literature examined found little to no data and a DPP was used to determine effect size (ES) and standard deviations (SDs) once 30 patients had been enrolled in each group. The DPP procedure was: 1) Determine the test statistic; 2) Identify the power formula most appropriate to the test statistic; 3) Determine the ES, variation and assumptions needed for the data-peek in the form required by the formula; 4) Construct a matrix of possible sample size values; and 5) Select a sample size that is obtainable and answers the research question. **RESULTS:** Data for group A demonstrated a mean reduction of 2.75% ±0.760, group B mean reduction of 3.01% ±0.636. Exact power analysis showed 113 subjects per group would be needed. A matrix of likely sample size based on these values ranged from 44 to 193 per group. Based on this DPP, a sample of 120 per group was selected as the sample size that would deliver clinically meaningful results. **CONCLUSIONS:** A DPP is useful in late phase research to define appropriate sample size where no data exist. It is important to note that DPP methods do not require significance testing, but the benefit is no need for a correction for multiple comparisons at the time of the final analysis.

PRM188
FAULTY CONNECTIONS: CAN CRITICISMS OF NETWORK META-ANALYSIS IN NICE SUBMISSIONS BE AVOIDED?
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OBJECTIVES: To assess 1) how network meta-analyses (NMAs) included within manufacturer submissions to the National Institute for Health and Care Excellence (NICE) have been criticised by its Evidence Review Groups (ERGs); 2) how some of these criticisms might be avoided in future submissions; and 3) the extent to which such avoidance might increase the likelihood of a new intervention being approved. **METHODS:** We reviewed the ERG reports of all NICE technology appraisals published since January 2007 to identify those where the manufacturer's submission included an NMA. Subsequently, all criticisms made by the ERG of such analyses were analysed to seek common themes; and assess how often any one type of criticism was associated with a rejection by NICE. **RESULTS:** A total of 181 NICE technology appraisal reports were evaluated. These covered 243 separate interventions, 83 (34%) of which were drugs for cancer. Overall 37–64% of submissions cited NMAs, of which 43–83% were criticised, with this proportion having increased over time. Avoidable criticisms related to flaws in the systematic review methodology used to identify relevant RCTs for the analysis; inappropriate pooling of data from heterogeneous studies; and use of suboptimal statistical approaches in conducting the NMA. Unavoidable criticisms related to the lack of RCTs available for competitor drugs in the population of interest. However, no association was found between flaws in the NMA and a decision by NICE not to approve the use of the intervention. Instead, such rejection was associated mainly with a lack of evidence of clinical efficacy or cost-effectiveness in the target population. **CONCLUSIONS:** Most criticisms of NMAs could be avoided by a more rigorous and transparent approach to conducting and reporting the underlying systematic review and statistical analysis. However, rejection of submissions remains a considerable risk where the underlying evidence is weak.

PRM189
METHODOLOGICAL CHALLENGES IN COMPARING TOPICAL THERAPIES IN DERMATOLOGY IN THE ABSENCE OF HEAD TO HEAD STUDIES
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OBJECTIVES: German HTA agency requires evidence about the additional benefit of a new pharmaceutical versus an appropriate comparator as basis for price negotiations. This is challenging when head-to-head studies (H2HS) or randomized placebo-controlled trials (RPCTs) are missing and particularly in dermatology, where topical therapies in registration trials are usually compared to their individual vehicle. The aim of this research was to describe different approaches to assess the additional benefit of a new topical therapy under these limitations. **METHODS:** For ingenolmebutate-gel (IMG) and the appropriate comparator diclofenac-hyaluronic-acid (DHA) bibliographic literature search was conducted for RCTs followed by sequential screening on H2HS, comparable endpoints, RPCTs, common bridge comparator, H2HS of vehicles alone, RPCTs of vehicles. The similarity of vehicles was assessed by comparison of efficacy and safety profile. The lack of H2HS demands to conduct the following approaches depending on the comparability of vehicles: 1. An adjusted indirect comparison due to Bucher 1997 (vehicles are placebo-like or adequately similar) 2. Linkage of direct comparisons due to Wells 2009 (possible when H2HS or RPCTs of vehicles are available) 3. Mixed treatment comparison (MTC) (prerequisites as mentioned for Bucher). **RESULTS:** 5 RCTs for IMG versus 3 RCTs for DHA were identified with comparable endpoints. No RPCTs for topical therapies or for their vehicles, no H2HS of vehicles, no bridge comparator and no clear evidence for the adequate similarity of both vehicles could be detected. Therefore, the prerequisites of all available statistical methods are not met and cannot thoroughly be applied. Notwithstanding these limitations, Bucher (RR[95%KI]: 4.14[2.03;8.47]) and MTC both favor IMG significantly while Wells showed non-inferiority (RR[95%KI]: 0.8[2,03;8,47]) in the primary endpoint of IMG versus DHA. **CONCLUSIONS:** A definition of adequate similarity for vehicles by German HTA agencies is needed to enable the use of methodologically sound indirect comparisons or MTCs in reimbursement dossiers.

PRM190
USE OF MULTIVARIATE BAYESIAN EVIDENCE SYNTHESIS TO REDUCE UNCERTAINTY AROUND CLINICAL EFFECTIVENESS AND QUALITY OF LIFE ESTIMATES
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OBJECTIVES: In health technology assessment, decisions about reimbursement of new health technologies are largely based on effectiveness estimates. These estimates are sometimes also used to predict the health-related quality of life outcomes, such as EQ-5D, as part of economic evaluation. However, sometimes these effectiveness estimates are not readily available. When many alternative instruments measuring these outcomes are being used (and are not all reported) or an extended follow-up time of clinical trials is needed to evaluate long-term endpoints (and drug development is at an early stage), data on relevant outcomes may be limited. The aim of this study was to develop methodology that would allow synthesis of all available evidence to assess interventions early and reduce uncertainty around relevant outcomes. **METHODS:** Bayesian multivariate meta-analysis